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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/829,481	04/10/2001	James K. Presnail	BB1441USNA	8059

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EXAMINER
KUBELIK, ANNE R

ART UNIT	PAPER NUMBER
1638	

DATE MAILED: 11/21/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

4+6

Office Action Summary	Application No.	Applicant(s)	
	09/829,481	PRESNAIL ET AL.	
	Examiner	Art Unit	
	Anne R. Kubelik	1638	

-- The MAILING DATE of this communication appears on the cover sheet with th correspondenc address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 September 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-8,12-16 and 22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8,12-16 and 22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *with the application* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *4 and 6* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's election without traverse of Group I and SEQ ID NO:3/4 in Paper No. 9 is acknowledged. The restriction is made FINAL.

2. The cancellation of claims 9-11 and 17-21 and the amendment of claims 1-7 and 15-16 requested in Paper No. 9, filed 3 September, 2002, have been entered. Claims 1-8, 12-16 and 22 are pending.

3. Reference FR 2 695 392 cited on the information disclosure statement filed 12 February, 2002, fails to comply with 37 CFR 1.98(a)(3) because it does not include a concise explanation of the relevance, as it is presently understood by the individual designated in 37 CFR 1.56(c) most knowledgeable about the content of the information, of this patent, which is not in the English language. It has been placed in the application file, but the information referred to therein has not been considered.

4. The draftsman has approved the drawings as submitted.

5. The title of the invention is not descriptive of the instant invention. A new title is required that is clearly indicative of the invention to which the claims are directed. Note that titles can be up to 500 characters long.

6. The abstract is not descriptive of the instant invention. A new abstract is required that is clearly indicative of the invention to which the claims are directed.

Claim Rejections - 35 USC § 112

7. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

8. Claims 1-8, 12-16 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are broadly drawn to a multitude of nucleic acids encoding proteins with defensin activity, wherein the protein has 80% identity to SEQ ID NO:1, recombinant DNA constructs comprising those nucleic acids, cells and plants comprising the construct, methods for transforming cells and plants with the nucleic acid, and a method of using the transformed cells to produce a protein with defensin activity.

The instant specification, however, only provides guidance for construction of cDNA libraries from *Vaejovis carolinianus* (Kentucky scorpion), *Scolopendra canidens* (centipede), and *Argiope* sp. (orb spider) and random sequencing of the clones (example 1); identification of cDNAs as potentially encoding defensins by BLAST comparison to sequence databases and identification of SEQ ID NO:3 from *V. carolinianus* as encoding a protein (SEQ ID NO:4) with 75.7% identity to a defensin from *Androctonus australis hector* (examples 2-3), and general guidance for expression of genes in monocots, dicots and microbes (examples 4-6).

The instant specification fails to provide guidance for isolation or construction of nucleic acids encoding proteins with defensin activity, wherein the protein has 80% identity to SEQ ID NO:1, recombinant DNA constructs comprising those nucleic acids, cells and plants comprising the construct, methods for transforming cells and plants with the nucleic acid, and a method of using the transformed cells to produce a protein with defensin activity.

It is not clear that the instant nucleic acid actually encodes a protein with defensin activity. The instant specification states that SEQ ID NO:4 has only 75.7% identity to the defensin from *Androctonus australis hector* (pg 24). The specification provides no evidence that SEQ ID NO:4 actually encodes a protein with defensin activity. Duggleby (1997, Gene 190:245-249) teaches, "the function of any DNA sequence, whose identity is based solely on homology, can only be proven by experiments designed to evaluate that function" (pg 248, left column, paragraph 4).

In the event that Applicant is able to overcome the enablement rejection as set forth above, the scope of enablement would still be limited to nucleic acids of SEQ ID NO:3.

The instant specification fails to provide guidance for making the nucleic acids that encode proteins with 80% identity to SEQ ID NO:4 and that encode defensins. While the specification on pg 7 suggests making conservative substitutions (*e.g.*, substituting one polar amino acid for another, or one acidic one for another), this method of making variants does not produce predictable results. Lazar et al (1988, Mol. Cell. Biol. 8:1247-1252) showed that the "conservative" substitution of glutamic acid for aspartic acid at position 47 reduced biological function of transforming growth factor alpha while "nonconservative" substitutions with alanine or asparagine had no effect (abstract). Similarly, Hill et al (1998, Biochem. Biophys. Res. Comm. 244:573-577) teach that when three histidines that are maintained in ADP-glucose pyrophosphorylase across several species are substituted with the "nonconservative" amino acid glutamine, there is little effect on enzyme activity, while the substitution of one of those histidines with the "conservative" amino acid arginine drastically reduced enzyme activity (see

Table 1). The specification does not teach which amino acids can tolerate amino acid substitutions and which cannot.

Given the claim breath, unpredictability, and lack of guidance as discussed above, undue experimentation would have been required by one skilled in the art to develop and evaluate defensin-encoding nucleic acids encoding proteins with 80% identity to SEQ ID NO:4. Making all possible single amino acid substitutions in an 61 amino acid long protein like that encoded by SEQ ID NO:3 would require making and analyzing 19^{61} nucleic acids; these proteins would have 98.4% identity to SEQ ID NO:4. Because nucleic acids encoding proteins with 80% identity to SEQ ID NO:2 would encode proteins with 12 amino acid substitutions, many more than 19^{61} nucleic acids would need to be made and analyzed.

Expressing pesticidal peptides in plants is unpredictable. Peptides that are effective pesticides when isolated and fed to insects do not function as pesticides when genes encoding them are transformed into plants. Pang et al (1992, Gene 116:165-172) teach that in tobacco plants transformed with a gene encoding the scorpion insectotoxin I_5A, the peptide is not correctly processed and the resulting plants had no paralytic effect on tobacco budworm (pg 170, right column). Barton et al (1993, US Patent 5,177,308) teach that a neurotoxin from *Androctonus australis hector* was unexpectedly not effective against tobacco hornworm when expressed in plants even though it was effective when the protein was topically applied to the hornworms (column 9, line 62, to column 11, line 7).

The specification does not teach to which insects plants transformed with SEQ ID NO:3 would be resistant.

As the specification does not describe the transformation of any plant with a gene encoding SEQ ID NO:4 or a protein with 80% identity to SEQ ID NO:4, undue trial and error experimentation would be required to screen through the myriad of nucleic acids encompassed by the claims and plants transformed therewith, to identify those with pathogen resistance, if such plants are even obtainable.

Given the claim breath, unpredictability in the art, undue experimentation, and lack of guidance in the specification as discussed above, the instant invention is not enabled throughout the full scope of the claims.

9. Claims 1-8, 12-16 and 22 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter that was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The claims are broadly drawn to a multitude of DNA molecules that encode defensins that have 80% sequence identity to SEQ ID NO:4. In contrast, the specification only describes a coding sequence from *V. carolinianus* that comprises SEQ ID NO:3. Applicant does not describe other DNA molecules encompassed by the claims, and the structural features that distinguish all such nucleic acids from other nucleic acids are not provided.

Hence, Applicant has not, in fact, described DNA molecules that encode defensins that have 80% sequence identity to SEQ ID NO:4 within the full scope of the claims, and the specification fails to provide an adequate written description of the claimed invention.

Therefore, given the lack of written description in the specification with regard to the structural and physical characteristics of the claimed compositions, it is not clear that Applicant was in possession of the genus claimed at the time this application was filed.

See *Univ. of California v. Eli Lilly*, 119 F.3d 1559, 43 USPQ 2d 1398 (Fed. Cir. 1997):

> The name cDNA is not in itself a written description of that DNA; it conveys no distinguishing information concerning its identity. While the example provides a process for obtaining human insulin-encoding cDNA, there is no further information in the patent pertaining to that cDNA's relevant structural or physical characteristics; in other words, it thus does not describe human insulin cDNA .... Accordingly, the specification does not provide a written description of the invention ....

and at pg 1406:

> a generic statement such as "vertebrate insulin cDNA" or "mammalian insulin cDNA," without more, is not an adequate written description of the genus because it does not distinguish the genus from others, except by function. It does not specifically define any of the genes that fall within its definition. It does not define any structural features commonly possessed by members of the genus that distinguish them from others. One skilled in the art therefore cannot, as one can do with a fully described genus, visualize or recognize the identity of the members of the genus. A definition by function, as we have previously indicted, does not suffice to define the genus because it is only an indication of what the genes does, not what it is.

See *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ 2d 1016 at page 1021:

> A gene is a chemical compound, albeit a complex one, and ... conception of a chemical compound requires that the inventor be able to define it so as to distinguish it from other materials .... Conception does not occur unless one has a mental picture of the structure of the chemical or is able to define it by its method of preparation, its physical or chemical properties, or whatever characteristics sufficiently distinguish it. It is not sufficient to define it solely by it principal biological property, *e.g.*, encoding human erythropoietin, because an alleged conception having no more specificity than that is simply a wish to know the identity of any material with that biological property.

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 14 and 22 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicant regards as the invention.

Claim 14 lacks antecedent basis for the limitation "the transformed plant cell" in line 2.

Claim 22 lacks antecedent basis for the limitations "the cultivated cells" in lines 3-4 and "the culture medium" in lines 4-5.

12. Claims 1-8, 12-16 and 22 are free of the prior art, given the failure of the prior art to teach or suggest an isolated nucleic acid encoding a protein with at least 80% identity to SEQ ID NO:4.

Conclusion

13. No claim is allowed.

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne R. Kubelik, whose telephone number is (703) 308-5059. The examiner can normally be reached Monday through Friday, 8:30 am - 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Amy Nelson, can be reached at (703) 306-3218. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 872-9307 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Anne R. Kubelik, Ph.D.
November 5, 2002

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